WHAT IS CLAIMED IS:

1. A method for making an infectious adenovirus which comprises contacting a cell or introducing into a cell:

(a) either (i) a first nucleic acid sequence encoding adenovirus sequences which, in the absence of intermolecular recombination, are insufficient to encode an infectious, replicable or packageable adenovirus, said first nucleic acid sequence comprising at least one site-specific recombinase recognition target site which is recognized by a site-specific recombinase or (ii) a first nucleic acid sequence encoding adenovirus sequences which are sufficient to encode an infectious, replicable or packageable adenovirus and comprising at least one site-specific recombinase recognition target site which is recognized by a site-specific recombinase, wherein contact of said first nucleic acid with said site-specific recombinase results in excision of sequences from said first nucleic acid sequence such that, in the absence of intermolecular recombination, said adenovirus of (ii) is rendered replication or packaging defective;

(b) a second nucleic acid sequence encoding adenovirus sequences which, in the absence of adenoviral replication factors provided in trans or intermolecular recombination with said first nucleic acid sequence, are insufficient to encode an infectious, replicable or packageable adenovirus, said second nucleic acid sequence comprising at least one recombinase recognition target site sufficiently identical with said recombinase recognition target site in said first nucleic acid as to be recognized by the same site-specific recombinase which recognizes said site-specific recombinase recognition target site in said first nucleic acid;

whereby said first and said second nucleic acid sequences, in combination and following site-specific intermolecular recombination, result in production of an infectious adenovirus, and wherein a site-specific recombinase which recognizes said site-specific recombinase recognition target sites is either (i) expressed by a cell into which said first and said second nucleic acids are introduced, (ii) operatively encoded by said first nucleic acid, said second

nucleic acid or both, or (iii) is provided in trans through expression from a third nucleic acid or is provided in trans as an active protein.

2. The method according to claim 1 wherein said second nucleic acid sequence is a plasmid comprising:

(i) all or most of the left ITR and the packaging signal contained within the leftmost approximately 350 nt of the adenovirus genome;

(ii) a polycloning site or a foreign DNA or an expression cassette; and

(iii) a *lox* P site 3' of said polycloning site, foreign DNA, or an expression cassette.

3. The method according to claim 1 wherein said first nucleic acid sequence is a plasmid containing a circularized adenovirus DNA molecule encoding adenovirus sequences which, in the absence of intermolecular recombination, are insufficient to encode an infectious, replicable or packageable adenovirus.

4. The method according to claim 3 wherein said plasmid includes a bacterial origin of DNA replication and an antibiotic resistance gene for selection in bacteria.

5. The method according to claim 3 wherein said adenovirus DNA has a deletion of an adenoviral packaging signal, or wherein said packaging signal is flanked on either side by at least one of said site-specific recombinase recognition sites.

6. The method according to claim 5 wherein said adenovirus DNA comprises (i) a deletion of, (ii) a modification in, or (iii) a flanking with a site-specific recombinase recognition site of, an adenoviral gene selected from the group consisting of adenoviral E1 sequences extending beyond said packaging signal, adenoviral fibre gene sequences, adenoviral E3 gene sequences, adenoviral E4 gene sequences, and combinations thereof.

7. A recombinant adenovirus vector system comprising:

(a) either (i) a first nucleic acid sequence encoding adenovirus sequences which, in the absence of intermolecular recombination, are insufficient to encode an infectious, replicable or packageable adenovirus, said first nucleic acid sequence comprising at least one site-specific recombinase recognition target site which is recognized by a site-specific recombinase or (ii) a first nucleic acid sequence encoding adenovirus sequences which are sufficient to encode an infectious, replicable or packageable adenovirus and comprising at least one site-specific recombinase recognition target site which is recognized by a site-specific recombinase, wherein contact of said first nucleic acid with said site-specific recombinase results in excision of sequences from said first nucleic acid sequence such that, in the absence of intermolecular recombination, said adenovirus of (ii) is rendered replication or packaging defective;

(b) a second nucleic acid sequence encoding adenovirus sequences which, in the absence of adenoviral replication factors provided in trans or intermolecular recombination with said first nucleic acid sequence, are insufficient to encode an infectious, replicable or packageable adenovirus, said second nucleic acid sequence comprising at least one recombinase recognition target site sufficiently identical with said recombinase recognition target site in said first nucleic acid as to be recognized by the same site-specific recombinase which recognizes said site-specific recombinase recognition target site in said first nucleic acid;

whereby said first and said second nucleic acid sequences, in combination and following site-specific intermolecular recombination, result in production of an infectious adenovirus, and wherein a site-specific recombinase which recognizes said site-specific recombinase recognition target sites is either (i) expressed by a cell into which said first and said second nucleic acids are introduced, (ii) operatively encoded by said first nucleic acid, said second nucleic acid or both, or (iii) is provided in trans through expression from a third nucleic acid or is provided in trans as an active protein.

8. The recombinant adenovirus vector system of claim 7 wherein said cell further expresses adenoviral E1.

9. The recombinant adenovirus vector system of claim 7 wherein said first plasmid and said second plasmid are cotransfected into said cell to produce an infectious virus vector comprising a left end, a polycloning site, foreign DNA, or an expression cassette derived from said second plasmid, joined to the remaining portion of the viral DNA derived from said first plasmid.

10. The recombinant adenovirus vector system according to claim 7 wherein said first nucleic acid sequence comprises a recombinase recognition site and a deletion in the adenoviral fibre gene.

11. A kit for construction of recombinant adenovirus vectors comprising:

(a) either (i) a first nucleic acid sequence encoding adenovirus sequences which, in the absence of intermolecular recombination, are insufficient to encode an infectious, replicable or packageable adenovirus, said first nucleic acid sequence comprising at least one site-specific recombinase recognition target site which is recognized by a site-specific recombinase or (ii) a first nucleic acid sequence encoding adenovirus sequences which are sufficient to encode an infectious, replicable or packageable adenovirus and comprising at least one site-specific recombinase recognition target site which is recognized by a site-specific recombinase, wherein contact of said first nucleic acid with said site-specific recombinase results in excision of sequences from said first nucleic acid sequence such that, in the absence of intermolecular recombination, said adenovirus of (ii) is rendered replication or packaging defective;

(b) a second nucleic acid sequence encoding adenovirus sequences which, in the absence of adenoviral replication factors provided in trans or intermolecular recombination with said first nucleic acid sequence, are insufficient to encode an infectious, replicable or packageable adenovirus, said second nucleic acid sequence comprising

at least one recombinase recognition target site sufficiently identical with said recombinase recognition target site in said first nucleic acid as to be recognized by the same site-specific recombinase which recognizes said site-specific recombinase recognition target site in said first nucleic acid; and

(c) a cell wherein, when said first nucleic acid sequence and said second nucleic acid sequence are cotransfected and recombined through the action of a recombinase which recognizes said recombinase recognition sites to produce a packaged and infectious adenovirus vector.

12. The kit according to claim 11 wherein said cell of (c) is selected from the group consisting of 293 cells expressing Cre, PER-C6 cells expressing Cre, 911 cells expressing Cre, and wherein said recombinase recognition sites are lox sites.

13. The recombinant adenovirus vector system according to claim 7 comprising:

(a) either (i) a first nucleic acid sequence encoding adenovirus sequences which, in the absence of intermolecular recombination, are insufficient to encode an infectious, replicable or packageable adenovirus, said first nucleic acid sequence comprising at least one site-specific recombinase recognition target site which is recognized by a site-specific recombinase or (ii) a first nucleic acid sequence encoding adenovirus sequences which are sufficient to encode an infectious, replicable or packageable adenovirus, said first nucleic acid sequence comprising (A) at least one restriction enzyme recognition site such that upon restriction of said nucleic acid with a restriction enzyme which recognizes said site, a site-specific recombinase recognition target site remains intact, but said adenovirus of (ii) is rendered replication or packaging deficient, or (B) wherein said nucleic acid comprises at least one site-specific recombinase recognition site which is recognized by a site-specific recombinase, wherein contact of said first nucleic acid with said site-specific recombinase results in excision of sequences from said first nucleic acid sequence

such that, in the absence of intermolecular recombination, said adenovirus of (ii) is rendered replication or packaging defective;

(b) a second nucleic acid sequence encoding adenovirus sequences which, in the absence of adenoviral replication factors provided in trans or intermolecular recombination with said first nucleic acid sequence, are insufficient to encode an infectious, replicable or packageable adenovirus, said second nucleic acid sequence comprising at least one recombinase recognition target site sufficiently identical with said recombinase recognition target site in said first nucleic acid as to be recognized by the same site-specific recombinase which recognizes said site-specific recombinase recognition target site in said first nucleic acid;

wherein said first and said second nucleic acid sequences, in combination and following site-specific intermolecular recombination, result in production of an infectious adenovirus, and wherein a site-specific recombinase which recognizes said site-specific recombinase recognition target sites is either (i) expressed by a cell into which said first and said second nucleic acids are introduced, (ii) operatively encoded by said first nucleic acid, said second nucleic acid or both, or (iii) is provided in trans through expression from a third nucleic acid or is provided in trans as an active protein.